ASBESTOS RELATED PLEURAL DISEASE DUE TO TREMOLITE CAUSES PROGRESSIVE LOSS OF LUNG FUNCTION

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ABSTRACT

123 patients in a private practice setting who were exposed to tremolite asbestos ~~in Libby, Montana, at the W R. Grace~~ vermiculite mine ~~and the environments of~~ Libby, Montana ~~were studied for progression of~~ loss of pulmonary function 94 of 123 patients had worsened vital capacity and the average age-corrected loss per year for vital capacity was 3 2%, total lung capacity 2 3%, and DLCO 3 3% These patients all had predominantly pleural disease with minimal to no interstitial disease The study ~~will~~ demonstrate the progressive nature of loss of pulmonary function in patients exposed to tremolite asbestos and their progressive loss of pulmonary function

INTRODUCTION

There has been a significant increase in this country in asbestosis and its various manifestations Increasing incidence of asbestosis related diseases due to exposures in the 1960s and 1970s are now becoming manifest Tremolite is an amphibole which has very little commercial value but is a contaminant in the mining of vermiculite This paper will reference the high incidence of asbestos related diseases and their progression associated with tremolite from a vermiculite mine owned by W R Grace corporation in Libby, Montana[1] The amphibole of the Libby mine has been characterized as tremolite, actinolite, richterite, and winchite It will be referred to as Libby tremolite or tremolite in the article

The vermiculite bed 6 miles north of Libby was discovered in the 1916 and mined initially for asbestos by the Zonolite Corporation and then subsequently for vermiculite It was mined by W R Grace & Co from 1963 to 1990 and was for a long period of time the world's largest producers of vermiculite

Vermiculite is a micacious silicate, which when heated expands to between 10 and 20 times its original proportions and is excellent as an insulator, soil conditioner and fertilizer additive

In the process of mining and processing this material, W R Grace Corporation had multiple sites in proximity to Libby The ore body contained 21 -26% tremolite[2] and was initially processed on the mountain The concentrated ore, which contained over 2-6% tremolite[2] was then loaded in railcars and shipped throughout the nation to the over 60 plus expansion plants operated for producing vermiculite insulation There was also a large expansion plant in downtown Libby as well as shipping facilities The finished product had up to 1-3% tremolite mixed with vermiculite[2]

W R Grace made vermiculite free to the community Many of the homes in Libby were insulated with vermiculite Vermiculite was placed on the ballfields, school track, and children played in piles of this vermiculite, which was lying around the various Grace facilities for many years The vermiculite was also used as insulation for plywood dryers in the lumber mills and was a particularly large contaminate in the rail yards where ore cars were loaded for shipping

Over 400 patients have been followed in a private practice setting, for up to 14 years Initially these were mostly employees of W R Grace but there was also a heavy

contamination of family members and more recently asbestos related diseases have been occurring in the general population of Libby

Because of those facts, the Agency for Toxic Substances and Disease Registry (ATSDR) a branch of the Communicable Disease Center (CDC) and the US Environmental Protection Agency (EPA) Region 8 in Denver, has performed an extensive screening in Libby, Montana In addition to the 400 cases that were present in this private practice, there is a large series of patients with asbestos related chest abnormalities numbering over 1000 at this point The incidence in the community of asbestos related diseases either manifested as overt asbestos disease or as abnormal chest x-rays is now estimated between 19 and 30 %[1] Although many of these patients are not sick as yet, this represents a significant environmental catastrophe and follow up of these patients for many years is going to be necessary

Because of the data in this private practice showing progression of the disease, a study was undertaken to review those patients who had been followed long enough to provide information concerning changes in pulmonary function

METHODS

153 patients have been followed for one or more years All of them have two or more sets of complete pulmonary function studies done with total body plethysmography and single breath carbon monoxide diffusion The studies prior to 1998 were done on a Sensormedics model 6200 Since 1998, studies have been done on Medgraphics model 1085 All studies were done before and after bronchodilator utilizing Albuterol The same technician was used throughout the entire period

For any patient, the first set of studies that were done and the last set prior to October 2001, were utilized to evaluate change in pulmonary function Normal values used were Knutson (1983) for spirometry[3] , Intermountain Thoracic Society (1984) for lung volumes[4], Miller (1983) for diffusion [5] All studies were reviewed to be certain the height and ages were correct and if errors in height were present they were corrected so that the first and last studies matched ATS standards were used throughout

30 patients were removed from the study for the following reasons Chronic obstructive pulmonary disease with elevated residual volumes, patients with intercurrent surgeries such as cardiopulmonary bypass or thoracic surgery for removal of neoplastic lesions, patients whose pulmonary functions were difficult to interpret because of patient unreliability and inability to meet ATS standards, and any other process thought to significantly alter the natural course of asbestos related disease Attempts were made to be certain that all patients in the study reflected the natural course of the disease The majority of the patients were ex-smokers 8 of 123 (7%) continued to smoke 86 (70%) were former employees of W R Grace 27 (22%) were family members of employees and 10 of 123 (8%) were characterized as environmental exposures 99 were males (80%), 24 females (20%) The average age was 66 years at first pulmonary function study

Since the patient values were all age corrected with the same predicted values used throughout, changes in the percentage of predicted reflected progression or changes of pulmonary function

Studies were then tabulated for the difference between the first and last study Change per year was calculated and all data was subjected to statistical analysis The

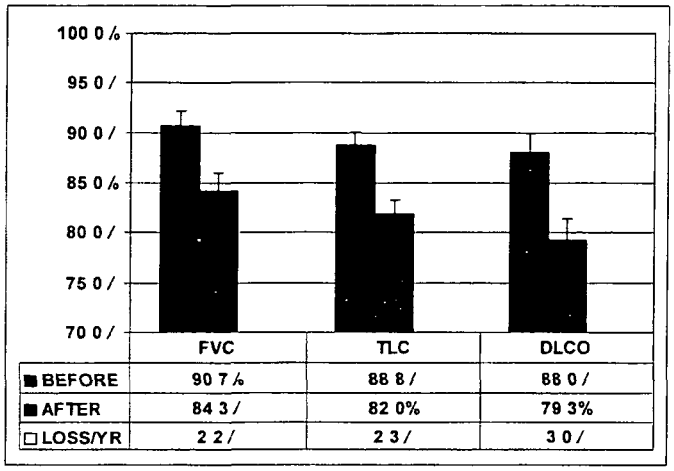
majority had pleural disease only 67 of 123 had no evidence on chest x-ray or high resolution CT scanning of any interstitial lung disease 56 patients had minimal and usually questionable evidence of interstitial disease and would be ILO graded as O/1 or 1/O

RESULTS

Using forced vital capacity as the primary measure of worsening of this disease, 94 of the 123 (76%) analyzed had worsening pulmonary function Those that did not were generally stable The amount of improvement in a few was minimal and may have been related to some co-existent bronchospasm Many of these patients after the initial study had been on bronchodilators because of bronchodilator responses on pulmonary function although none had carried a diagnosis of bronchial asthma

The parameters that were felt to be most valuable for analysis were the forced vital capacity (FVC) (taking the best available number from each set), total lung capacity (TLC)and the single breath diffusion capacity (DLCO) In the whole group of 123 patients (including those with improved FVC), over an average of 35 months, the average loss per year was 2 2 % for FVC, 2 3% for TLC, and 3 0% for DLCO Fig 1)

% LOSS OF PULMONARY FUNCTION ALL 123 PATIENTS (AVERAGE 35 MONTHS) (p< 001)

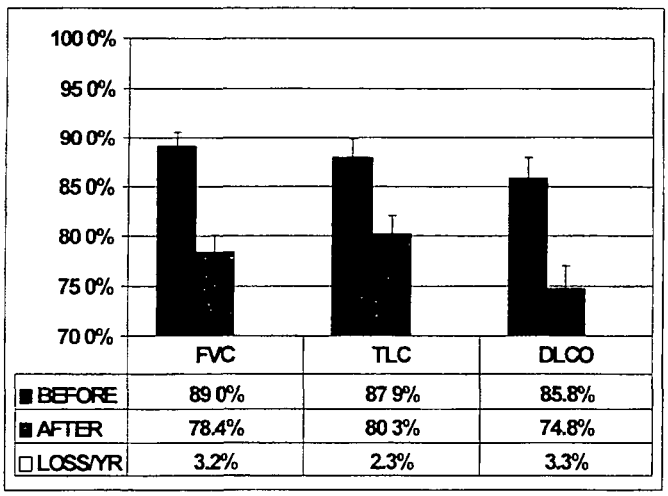


	FVC	TLC	DLCO
BEFORE	90 7 /.	88 8 /	88 0 /
AFTER	84 3 /	82 0%	79 3%
LOSS/YR	2 2 /	2 3 /	3 0 /

FIG 1

Analyzing the 94 of the 123 who had actually worsened forced vital capacity, the loss for FVC was 3 2%, TLC 2 3%, DLCO 3 3% (Fig 2)

% LOSS OF PULMONARY FUNCTION 94/123 PATIENTS WITH WORSE FVC (AVERAGE 40 MONTHS) (p< 001)



	FVC	TLC	DLCO
BEFORE	89 0%	87 9%	85.8%
AFTER	78.4%	80 3%	74.8%
LOSS/YR	3.2%	2.3%	3.3%

FIG 2

79 of 123 patients had greater than 1% loss of FVC per year and their average loss of rate of pulmonary function was 3 6% for FVC per year, 2 5% for TLC, and 3 5% for DLCO (fig 3)

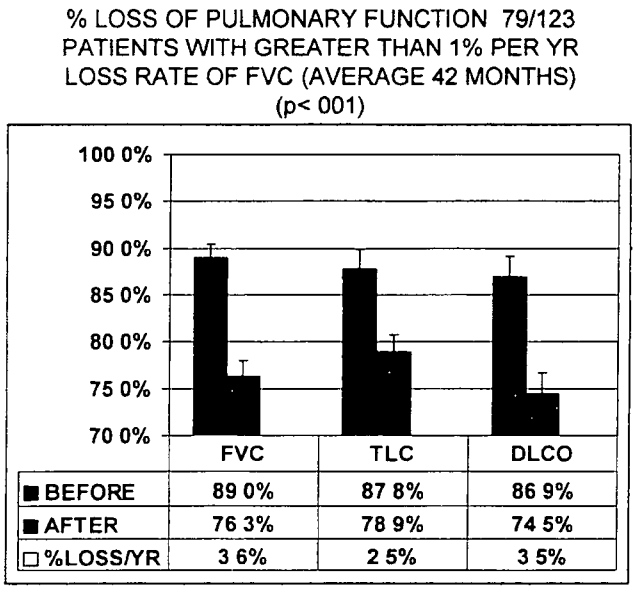
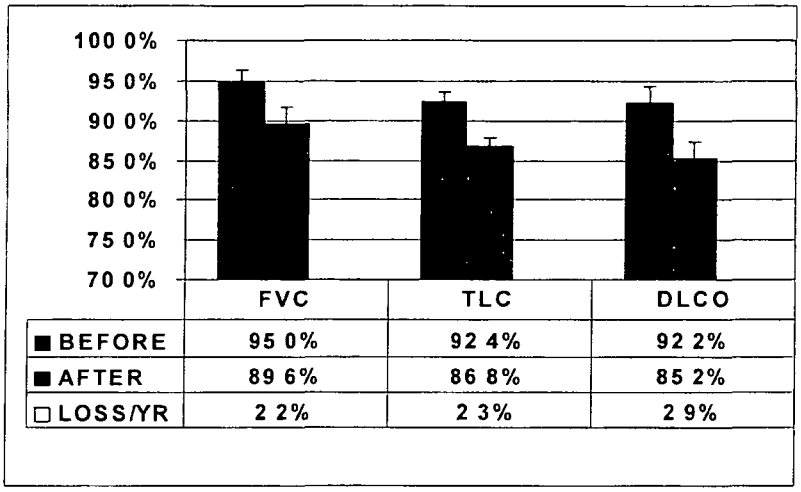


FIG 3

It was not possible to differentiate this group of more rapid loss from the remainder, either radiographically , by age, or exposure history

The 67 patients with only pleural disease on the chest x-ray and no interstitial disease,losses of FVC-2 2%, TLC-2 3%, DLCO-2 9% were recorded

% LOSS PULMONARY FUNCTION 67/123 PATIENTS (AVERAGE 29 MONTHS) PLEURAL DISEASE ONLY (p=< 001)



	FVC	TLC	DLCO
■ BEFORE	95 0%	92 4%	92 2%
■ AFTER	89 6%	86 8%	85 2%
□ LOSS/YR	2 2%	2 3%	2 9%

FIG 4

These results are very similar to those of the entire 123 patients,(compare fig 1 to fig 4)

All values were statistically significant at P=< 001 The statistical methods utilized was two factor, repeated measures of analysis of variance (time by time difference) There did not appear to be any difference between the patients who had some minor degree of interstitial disease versus those who had no obvious evidence of interstitial disease either by chest x-ray or by CT scanning It is also noted that in the entire group the decline in the diffusion capacity was more rapid than the decline in either the FVC or TLC 76% of these 123 patients from Libby, Montana with predominate pleural disease only, have progressive loss of lung function at the rate of up to 3% per year No obvious discernable pattern was noted as far as other initiating events and in the

majority of these patients there were minimal changes in the chest x-ray through the period of time they were losing pulmonary function There are some notable exceptions when pleural effusions occurred It is unclear why there was not progression in the other 24% of the patients There are no obvious differences between the two groups and that study will be ongoing

DISCUSSION

The progression of loss of pulmonary function in 76% of the 123 patients with pleural disease followed in this group of patients from Libby is far higher than what has been previously reported with other forms of asbestos Progression of asbestos disease in patients with exposure to chrysotile asbestos is well documented Jones[6] (1989), demonstrated declines in FVC and FEV1 in men who had progression of pleural thickening 31% of their group showed progression of parenchymal small opacities in patients with pleural thickening and smoking was not a significant determinant of pleural progression Crocidolite was present in one of the two plants studied and there was a higher rate of progression in those plants in which crocidolite was present Death due to pleural thickening has been described by Miller and Miller[7] (1993), and decreases in vital capacity by Lillus[8] (1991) and Schwartz[9 10] (1993) Miller[7] felt that patients with longstanding clinically inconsequential plaques remain at risk for diffuse pleural thickening and associated impairment of pulmonary function, which seems to be documented in this group of patients with tremolite exposure Olson[11] (1985) described four year declines in FVC and FEV_1 in a group of asbestos cement workers Rom[12] (1992) studied 77 asbestos insulators and found losses of the FVC averaged 92 cc per year, FEV_1 66 cc per year, and TLC 14 cc per year Kouris[13] (1991) found decreased pulmonary function associated with pleural plaques and more significantly with diffuse pleural thickening Schwartz [9] (1990) demonstrated loss of FEV_1 and FVC associated with both plaques and diffuse pleural thickening and they concluded that "pleural fibrosis among asbestos exposed patients is an independent predicter of spirometric patterns

Author (n) Exp | Duration | # | 2 Loss

consistent with restrictive lung function Brodkin (1996)[14] further correlates loss of pulmonary function associated with increasing respiratory symptoms

There are fewer articles on exposure to amphiboles Shephard[15] (1996) showed progression of pleural and parenchymal abnormalities associated with amosite Sluis-Cremer[16] (1989) studied crocidolite workers in South Africa, and was able to demonstrate that once a dose of amphibole asbestos sufficient to initiate disease had been retained it was a naturally progressive process, Cookson[17] (1986) studying crocidolite workers demonstrated the disease was active even after more than three decades and there was continued progression over a 35 year period Erlich[18] (1992) demonstrated in amosite exposed workers there was progression of pleural abnormalities 20 years after exposure They found exposure of as little as one month was sufficient to produce radiologic signs of parenchymal and pleural fibrosis and progression was detectable greater than 20 years after the end of exposure Locke[19] (1984), studying workers exposed to tremolite asbestos from the Grace mine in Libby, Montana, has previously demonstrated extensive pleural changes on chest radiographs Many of patients in his study in 1984 are probably in this current study but at the time seen in 1984 had not yet reached the point of rapid progression of their disease

CONCLUSIONS

This study demonstrates that pleural disease is associated with continued ongoing progression of loss of pulmonary function in a group of patients exposed to tremolite from approximately 1950 to 1975 and are continuing to progress up to 40 years after their exposure The studies quoted above document progression of both interstial disease and pleural disease, both radiographically and functionally, but none document the rapid

progression of loss of pulmonary function in such a large group of patients with predominantly pleural disease McDonald[20] (1999) speculated on tremolite's increased fibrogenicity and it would appear that tremolite is much more fibrogenic than chrysotile, and possibly more so than the other amphiboles as well

Exposure histories for this group are complex because for the most part there was continuous exposure throughout this entire period that they lived in Libby whether they were mine workers, family members of workers, or community members living near the vermiculite processing facilities

This study demonstrates that the number of patients progressing is much higher than has previously been reported in prior studies with either chrysotile or amphibole asbestos exposure Tremolite asbestos related pleural disease is a progressive and disabling disease Lincoln County, Montana, (where Libby is the county seat) has the highest mortality rate from asbestosis in the nation It is apparent from this data that the majority of the 1500 persons who have radiologic changes of asbestos disease are likely to have progressive lung disease This is going to require long-term followup for the Libby exposed community for 30 or 40 years because the exposures have been ongoing to at least the early 1990s Assuming a latency period of between 20 and 30 years to significant disease it is not unreasonable to expect that the people of Libby, Montana will still be dealing with loss of pulmonary function, pleural effusions, malignancies, and mesotheliomas related to these exposures for many decades

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